CONCLUSIONS AND RECOMMENDATIONS

The International Programme on Chemical Safety (IPCS)

WHO ILO UNEP

IPCS Project on the Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals

GENERAL CONCLUSIONS AND RECOMMENDATIONS[1] OF AN IPCS INTERNATIONAL WORKSHOP ON SKIN SENSITIZATION IN CHEMICAL RISK ASSESSMENT

17-18 October 2006, Berlin, Germany

Preamble

WHO/IPCS, in conjunction with the German Federal Institute for Risk Assessment, convened an international workshop on skin sensitization in chemical risk assessment in Berlin, Germany from 17-18 October 2006. The workshop focused on skin sensitization arising from exposure to chemicals. It aimed to evaluate experimental techniques for both hazard identification and hazard characterization, with the ultimate goal to evaluate their ability to produce data to inform risk assessment, including provision of dose-response information and information relating to sensitive sub-populations. The workshop focused on whether it is possible to distinguish between chemicals with a high potency to elicit allergic skin reactions and those with a low potency. Emerging approaches, such as Structure Activity Relationships (SAR) were explored. The meeting also explored whether experimental approaches used in identifying skin sensitization could inform approaches to identify chemicals with the potential for respiratory tract sensitization. The full report of this workshop will be published. The list of participants appears at Annex 1.

Conclusions

The relative ability of a chemical to induce sensitization is an intrinsic property of the chemical, and is determined by the amount of chemical *per unit area* required for the acquisition of skin sensitization in a previously naïve individual.

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[1] This report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization.

The Local Lymph Node Assay (LLNA) is the preferred test method for assessing skin sensitization ability of chemicals in view of animal welfare considerations. It has been validated for the purpose of hazard identification. However, presently there is still a need for guinea- pig tests. Guinea-pig tests may still have a place for the testing of aqueous solutions, extracts, fabrics, mixtures and preparations. When conducting guinea-pig assays the Buehler assay is preferred over the Guinea-pig Maximization Test (GPMT) from an animal welfare point of view. However, the GPMT is generally considered to be more sensitive than the Buehler Assay, for which reason some regulatory authorities prefer the GPMT.

(Quantitative)SARs and expert systems for identification of sensitizing capacity have not been validated to date, but may be used as part of a weight of evidence approach for identifying the sensitizing capacity of chemicals. There are certain local (Q)SARs that can be used for a small range of chemicals. However, these are currently insufficient to cover the full range of chemicals.

No in vitro assay systems for identification of sensitizing capacity have been validated to date. Some of these systems may be useful in a weight of evidence approach or as a preliminary screen.

Any test of skin sensitizing capability that includes dose-response assessment can be used to assess potency. Currently the LLNA is the most appropriate assay for single chemical substances, as it is the only test for which guidelines indicate to include dose-response assessment. Guinea-pig data may also be used to categorize a chemical according to its skin sensitizing potency. It is acknowledged that categorization of skin sensitizing potency is associated with a degree of uncertainty. Neither the approach using the LLNA, nor the approach using guinea-pig data have been validated for the purpose of assessment of potency.

Elicitation responses depend on several factors, among which are potency of the allergen and exposure conditions. Even though potency cannot be directly derived from human elicitation data, a low elicitation threshold is suggestive of a high potency. Where possible, attempts should be made to use clinical data for quantitative risk assessment.

The suitability of test methods for mixtures and preparations, including assessment of skin sensitization induction potency, is not established for any sensitization assay.

Elicitation thresholds cannot be determined on the basis of skin sensitizing potency.

Although respiratory allergens tested so far were positive in current tests evaluating skin sensitization potential, skin sensitization potency data available from current test methods do not predict respiratory sensitization potency.

Recommendations

There is a need for a standardized system of classifying and determining limits according to potency.

The use of the LLNA for potency categorization of induction of skin sensitization needs to be validated. An abbreviated test validation approach may be appropriate to assess the validity of potency assessment based on the LLNA and its appropriateness for predicting sensitizing induction potency in humans.

It is recommended to derive dose-response curves from patch testing and/or open testing in individuals diagnosed with contact allergy, and thereby establish a threshold which can be used to derive a point of departure/risk assessment.

Existing human data on variability in individual thresholds should be evaluated to derive adjustment factors for risk assessment.

It is recommended that further studies are carried out regarding potency ranking of chemicals according their potency to elicit allergic responses in individuals diagnosed with contact allergy.

Comparison of information on responses after occluded versus non-occluded exposures, and single versus repeated exposures, should be done to inform adjustment factors for risk assessment that may account for specific exposure conditions.

Methodology to assess skin penetration, deposition and metabolism needs to be further advanced.

The LLNA needs to be further developed with a view to testing of aqueous solutions, preparations and complex mixtures.

The effects of irritant activity in the LLNA should be further explored.

It is recommended that non-radioactive active forms of the LLNA, or LLNA-type assays that use reduced amounts of radioactivity get more attention.

It is recommended that QSAR models need to be further developed, and the applicability domain of each model needs to be established.

Approaches to evaluate respiratory sensitization induction potency need to be developed.

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